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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/680,963	10/07/2003	Piotr Bobrowicz	GFI-108	6071

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EXAMINER	
QIAN, CELINE X	
ART UNIT	**PAPER NUMBER**
1636	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/20/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/680,963	BOBROWICZ ET AL.	
	Examiner	Art Unit	
	Celine X. Qian Ph.D.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-54* is/are pending in the application.

4a) Of the above claim(s) *1-12,18-21,25-31 and 40-54* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13-17,22-24 and 32-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *15 December 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1203, 0306*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-54 are pending in the application.

Election/Restrictions

Applicant's election with traverse of Group II in the reply filed on 2/2/07 is acknowledged. The traversal is on the ground(s) that the invention of groups II and V are not distinct from each other because they are related to lower eukaryotes comprise GnTIII activity. Applicants further assert that the invention of group II is an obvious variation of group V, wherein a search of group II will necessarily include references that relate to cells with GnTIII activity – including cells which additionally contain mannosidase activity. Applicants further assert that the invention of groups III and IV are not distinct from each other because they are obvious variants of each other. Moreover, Applicants assert that the invention of groups II-V overlap in scope and should be contained in the same group because lower eukaryotic host cells of groups II and V can produce glycoproteins having bisected glycans, are coextensive with the lower eukaryotic cells of groups III and IV that contain bisected glycoproteins. Applicants request the rejoining of groups II-V.

The above arguments are found partially persuasive. Applicants' admission that the invention of groups II and V is obvious variants of each other serves the basis for the rejoinder of groups II and V. Based on this assertion, it is interpreted that that the cells comprising GnTIII would either also comprise mannosidase or it would have been obvious for such cells to comprise mannosidase. Applicants' admission that the invention of groups III and IV is obvious variants of each other serves the basis for the rejoinder of groups III and IV. Based on this assertion, it is interpreted that it would have been obvious to cells comprising Man5GlcNAc2 to

produce bisected glycan. However, the invention of groups II, V and III, IV are patentably distinct from each other because they are not drawn to obvious variants of each other. A search or the former is not coextensive with the latter because a lower eukaryotic cell comprising bisected glycan or Man5GlcNAc2 does not require GnTIII activity. As such, the invention of groups II-V will not be rejoined.

Accordingly, claims 1-12, 18-21, 25-31 and 40-54 are withdrawn from consideration for being directed to non-elected subject matter. Claims 13-17, 22-24, 32-39 are currently under examination.

Claim Objections

Claims 22-24, 36-39 are objected to for containing non-elected subject matter. Amending the claims such that they are only directed to elected inventions is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 13-17, 22-24, 32-39 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The written description requirement is set forth by 35 U.S.C. 112, first paragraph which states that the: "*specification* shall contain a written description of the invention. . .[emphasis added]." The written description requirement has been well established and characterized in the case law. A specification must convey to one of skill in the art that "as of the filing date sought, [the inventor] was in possession of the invention." See *Vas Cath v. Mahurkar* 935 F.2d 1555, 1560 19 USPQ2d 1111, 1117 (Fed. Cir. 1991). Applicant may show that he is in "possession" of the invention claimed by describing the invention with all of its claimed limitations "by such descriptive means as words, structures, figures, diagrams, formulas, etc., that fully set forth the claimed invention." See *Lockwood v. American Airlines Inc.* 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997).

In analyzing whether the written description requirement is met, it is first determined whether a representative number of species have been described by their complete structure. Next, it is determined whether a representative number of species have been sufficiently described by other relevant identifying characteristics. The claimed invention is drawn to a lower eukaryotic cell comprising an N-acetylglucosaminyltransferase III activity, or additionally having either GnT I, II, or mannosidase activity, wherein the cell may or may not be deficient in an enzyme that have mannosyltransferase activity. The specification discloses that a lower eukaryotic cell encompasses any eukaryotic cell which ordinarily produces high mannose containing N-glycans, including animal, plant, uni and multicellular fungal and algal cells. The claimed genus of lower eukaryotic cells thus encompasses a large number of cells of different species having very different glycosylation pathways from each other which either naturally comprise the GnTIII and other recited enzymatic activity or have been genetically modified to

express such activity. The specification discloses that the claimed genus of lower eukaryotic cells are used for producing recombinant polypeptides that with glycosylation structure similar to those find in human cells such as a bisected N-glycan. However, the specification only discloses the genetic modification of yeast strains including K. lactis and P. pastoris to eliminate the mannosyltransferase that is responsible for high mannose glycosylation pattern, and subsequently introducing fusion proteins comprising 1,2 mannosidase, GnTI, II, III and proper localization signal to said yeast strains that results in the production of predominantly bisected N-glycan. The specification fails to teach yeast cells or other lower eukaryotic cells that naturally express said enzymatic activity, other lower eukaryotic cells that have been genetically modified to comprise said enzymatic activity, or yeast cells comprising the GnTIII enzymatic activity alone that would produce a bisected N-glycan. The state of art at the time of filing teaches that the glycosylation process and the enzymes involved in this process differs in different species of host cells. Lower eukaryotic yeast or fungal cells produces N-glycan with high mannose structure which would not result in the production of complex or hybrid N-glycan as mammalian cells (see Hamilton et al. Science, 2003, Vol 301, pages 1244-1246). This is result from the initial glycosylation activity of 1,6 mannosyltransferase in such cells, and the resulting high mannose structure cannot form Man5GlcNAc2, a precursor for complex N-glycan formation. Insect cells do not form complex N-glycan as mammalian cells but form paucimannosidic N-glycan. However, insect cells do not lack Man5GlcNAc2 structure (see Altmann et al. Glycoconjugate Journal, 1999. Vol 16, 109-123). Recombinant proteins produced in plant has divergent N-glycan structure which include high mannose type N-glycans from Man5GlcNAc 2 to Man8GlcNAc2 and complex N-glycan with beta 1,2 xylose and alpha 1,3

fucose residue (see Bardor et al. Trends in Plant Science, 1999. Vol 4, No.9, pages 376-380). Recombinant glycoprotein produced in non-human mammalian cells naturally have complex N-glycan structure. Strasser et al. (Biochem J. 2005, Vol 387, pages 385-391) teach that Arabidopsis thaliana plants lack complex N-glycans due to N-acetylglucosaminyltransferase I deficiency. Chui et al. (Cell, 1997, Vol 90, pages 157-167) teach that mice lack alpha-mannosidase II result in the loss of N-glycan in erythrocytes. The prior art also teaches the mere presence of the Man5GlcNAc2 within cell is not sufficient for producing complex N-glycan because the correct isoform is required for the subsequence enzymatic action of GlcNAc transferase I. In view of the teaching from the prior art, the formation of complex N-glycan in cells from different species requires a cascade of enzymatic actions, each is different from the other and produces complex N-glycan with different structure. The specification only teaches a method of producing bisected N-glycan in yeast by knocking out genes that are responsible for producing high mannose structure, and subsequently introducing enzymes necessary for the complex N-glycan formation, wherein the production of the complex N-glycan in said host cells is a result of concerted action of the combined genetic modification. The specification fails to describe other lower eukaryotic cells comprising the recited enzymatic activity either naturally or genetically modified, that can produce bisected N-glycan. In view of the broad claimed genus of eukaryotic cells, the specification fails to describe a representative number of species by their complete structure, nor other identifying characteristics. Therefore, the specification does not adequately described the claimed genus of lower eukaryotic cells.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 13-17, 22-24, 32-39 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claims 13-17, 22-24, 32-39, the recitation of "a lower eukaryotic host cells comprising an...activity" renders the claims indefinite because it is unclear what is the nature of the activity Applicants are referring to. In other word, it is unclear whether Applicants are referring to one of the enzymatic activity (i.e. binding or catalytic activity), the transcriptional activity, or the translational activity. As such, the metes and the bounds of the claims cannot be established. It would be remedial to recite "the acetylglucosamyltransferase III activity."

Regarding claim 15, the recitation of "the activity is substantially intracellular" renders the claim indefinite because it is unclear whether it means the enzyme is active only inside the cell or both intra or extracelluarly.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celine X. Qian Ph.D. whose telephone number is 571-272-0777. The examiner can normally be reached on 9:30-6:00 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Celine X Qian Ph.D.
Examiner
Art Unit 1636

CELINE QIAN, PH.D.
PRIMARY EXAMINER